UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,596	03/01/2002	Mark G. Currie	SEPR-P01-051	7919

28120 7590 03/30/2004

ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 03/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/087,596	CURRIE ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *4 and 10-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-9 and 14-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicants' Reply under 37 CFR 1.111 filed January 15, 2004 is acknowledged. Claims 1-40 are canceled. Claims 1-39 remain under consideration to the extent they read on the elected species, a nefazodonoid and a fluoxetinoid. Accordingly, claims 4 and 10-13 remain withdrawn from consideration by the Examiner as being drawn to non-elected inventions.

Applicants argue claims 4 and 10-13 are contained in Group I of the Restriction Requirement. Under 37 CFR 1.142(b), claims are withdrawn from consideration when directed to non-elected inventions.

An Information Disclosure Statement filed January 15, 2004 is further acknowledged and has been reviewed.

Claim 17 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n).

Subsequent to the cancellation of claim 40, the objection to the disclosure is moot.

Claims 7 and 39 were rejected in the last Office Action under 35 U.S.C. 112, second paragraph, for being indefinite.

Following the deletion of the recitations beginning with the term "preferably", the rejection of claim 7 is withdrawn. The rejection of claim 39 as failing to define the invention properly is withdrawn upon consideration that the claim is directed to a method for preparation.

Claims 1-3, 5, 7, 14-18 and 25-31 were rejected in the last Office Action under 35 U.S.C. 112, first paragraph, as lacking a clear written description of the invention of both pharmaceutical combinations other than nefazodone and fluoxetine and any 5-HT receptor-mediated disorders.

Applicants argue multiple nefazodonoids and SRI's are recited in the specification. Applicants hypothesize "one of skill in the art *would anticipate* that the same benefit would be achieved with SRI's other than fluoxetine and nefazodonoids other than nefazodone". Applicants refer to various parts of the specification which describe what is generally known in the art as conditions and disorders that are treated through administration of the claimed compounds.

Applicants' arguments are persuasive and this rejection of record is withdrawn.

Claims 26-34 were rejected in the last Office Action under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to make and practice the invention. It was asserted the claims are directed to methods for treating any 5-HT receptor-mediated disorder comprising co-administering a nefazodonoid and a serotonin reuptake inhibitor (SRI).

Applicants argue the nefazodonoid is administered at a dosage below the necessary dosage to inhibit serotonin reuptake to a therapeutically effective extent in the absence of the SRI.

The specification provides no example or support for the claimed critical limitation for the combination of a nefazodonoid and any serotonin reuptake inhibitor wherein the

nefazodonoid is administered at a dosage below the necessary dosage to inhibit serotonin reuptake to a therapeutically effective extent in the absence of the SRI. The determination of the dosage involves parameters as the renal and hepatic function of the patient, the existence of other pathologies, age, weight and potential drug interactions. Only a general disclosure that nefazodone is administered below 100 mg/day and fluoxetine is administered below about 50 mg/day is provided. There is no nexus established between a particular 5-HT receptor-mediated disorder and clear dosages of the two active drugs.

Accordingly, the rejection of claims 26-34 of record under 35 U.S.C. 112, first paragraph, is maintained.

Claims 1-3, 5-9 and 14-40 were rejected in the last Office Action under 35 U.S.C. 103 as being unpatentable over Fava, M., J. Clin. Psychiatry, in view of the web site Mhi Ask the Expert – SSRIs and Nefazodone.

It was asserted Fava teaches an augmentation strategy via the administration of nefazodone and selective reuptake inhibitors. The secondary reference teaches the combination of 50 mg of nefazodone with 5 mg of fluoxetine to treat refractory depression.

Applicants argue the references do not teach or suggest formulating nefazodone with an SRI in a pharmaceutical preparation; nefazodonoid is administered at a dosage below the necessary dosage to inhibit serotonin reuptake to a therapeutically effective extent in the absence of the SRI; Fava teaches a nefazodone dosages that are higher than those claimed; and, the references caution serotonin syndrome risk.

Applicants' arguments have been given careful consideration but are not found persuasive. The rejection is repeated for the reasons of record.

It is noted the open language in claims 1, 19 and 25 does not preclude the addition of any number of other active ingredients in the claimed preparation or kit.

Table 1 on page 27 of the Fava reference points out both advantages and disadvantages of combination therapy of nefazodone and SRI's. Despite a potential, and rare occurrence of serotonin syndrome when higher dosages are administered, there are benefits taught by Fava in combination therapy. Serotonin reuptake inhibitors have been reported to be useful in augmenting other serotonin reuptake inhibitors. Further, Fava teaches nefazodone may help manage sexual dysfunction that is induced by serotonin reuptake inhibitors. In view of combined teachings of the references, one skilled in the art would have been motivated to prepare a pharmaceutical composition comprising about 50 mg of nefazodone and about 5 mg of fluoxetine, to treat depression in a patient experiencing sexual dysfunction when receiving fluoxetine therapy. Nefazodone and fluoxetine have somewhat different modes and spectra of action. The secondary reference teaches 50 mg of nefazodone and 5 mg of fluoxetine, amounts that meet the requirement in the specification that the nefazodonoid is administered at a dosage below the necessary dosage to inhibit serotonin reuptake to a therapeutically effective extent in the absence of the SRI. Nefazodone is administered below 100 mg/day and fluoxetine is administered below about 50 mg/day. It would have been reasonable to expect lower doses of the active agents would result in less

occurrences of serotonin syndrome. In all 5-HT receptor-mediated disorders it would have been reasonable to expect only the lowest effective doses would be administered.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication should be directed to Phyllis G. Spivack at telephone number 571-272-0585.

Phyllis Spivack

Phyllis G. Spivack
Primary Examiner
Art Unit 1614

March 28, 2004

PHYLLIS SPIVACK
PRIMARY EXAMINER